

Arylation of 1,2,4-Triazines in the Presence of AlCl_3

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This paper presents a method for introducing toluene and bromobenzene moieties into 1,2,4-triazines as an alternative to cross-coupling reactions. It is demonstrated that the C=N bond of a wide range of 1,2,4-triazines undergoes addition of arenes in the presence of AlCl_3 .

Key words: Arylation, 1,2,4-Triazine, Aluminum Chloride

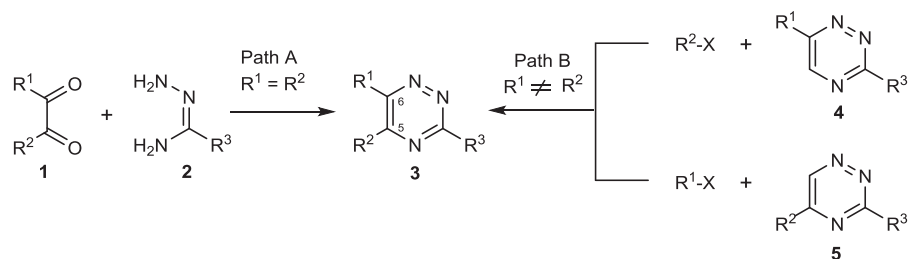
Introduction

The structure of 1,2,4-triazines is analogous to that of nucleobases, which encourages an ongoing search of bioactive compounds among them. Recent publications devoted to 5,6-biaryl derivatives of 1,2,4-triazines describe them as potential adenosine A_2A receptor antagonists (anti-Parkinsonism) [1] as well as neuroprotective [2, 3] and anti-tumor agents [4, 5]. These substances are also known to inhibit thrombocyte aggregation [6] and to possess anti-inflammatory [7–9], antidepressant [10], antibacterial [11], herbicidal [11], fungicidal [11, 12], and pesticidal [11, 13] properties.

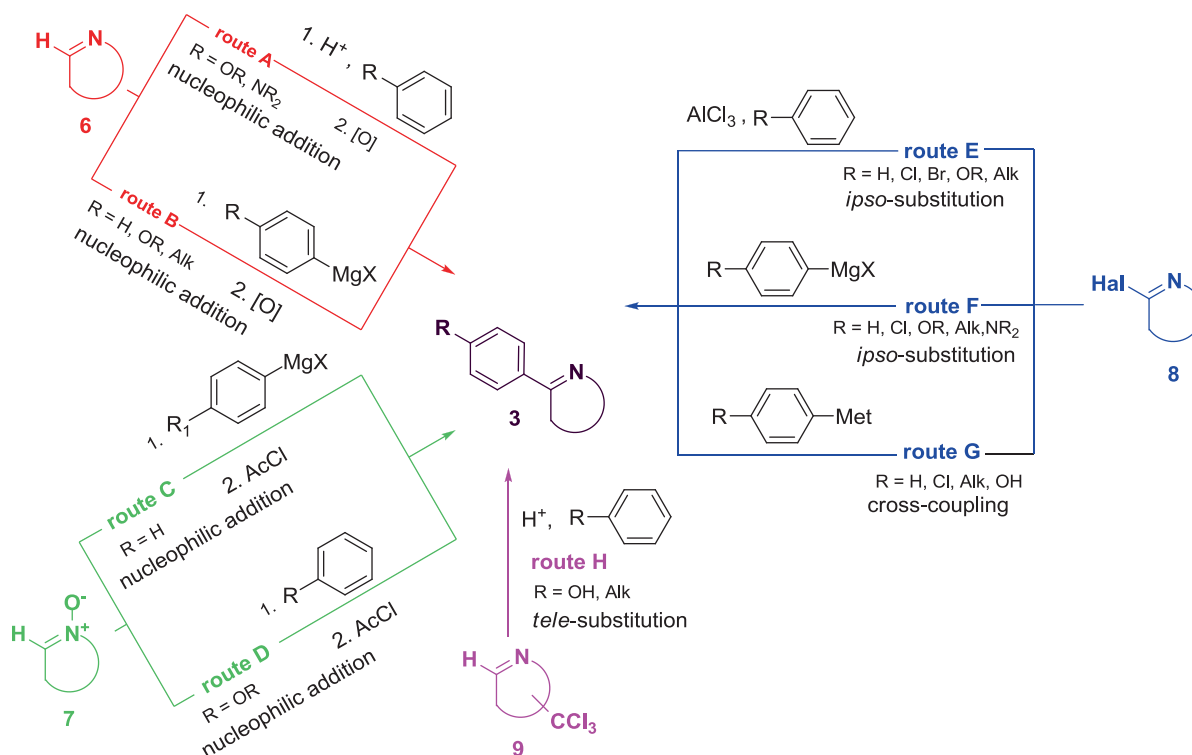
A general synthetic pathway towards 1,2,4-triazines **3** involves condensation of 1,2-dicarbonyl compounds **1** with amidrazones **2** (Path A, Scheme 1) [14]. This approach is very convenient for the synthesis of 1,2,4-triazines bearing identical substituents at C(5) and C(6). However, for 1,2,4-triazines with different substituents at these positions this method is challenging due to the formation of mixtures of isomeric 1,2,4-triazines from unsymmetrical 1,2-dicarbonyl compounds ($\text{R}^1 \neq \text{R}^2$) (Scheme 1) [15–18].

The current paper is devoted to the synthesis of 5,6-diaryl derivatives of 1,2,4-triazines **3** with $\text{R}_1 \neq \text{R}_2$ (Path B, Scheme 1). For this objective there are currently four possible starting triazine substrates available (Scheme 2). First, it is 1,2,4-triazine (**6**) with an unsubstituted carbon atom. It is known that introduction of arenes with strong electron-donating groups

(e. g. phenols and anilines) into 1,2,4-triazines can be achieved by activation of the latter with acids, which leads to the formation of triazinium cations and subsequent oxidation of the formed dihydro intermediates (route A, Scheme 2) [14, 19, 20]. However, no 5,6-biaryl derivatives have been synthesized *via* this route. Increasing the reactivity of arenes by conversion to Grignard reagents allows to perform reactions with non-activated 1,2,4-triazines (route B, Scheme 2) [21–24] and even 1,2,4-triazin-4-oxides **7** (route C, Scheme 2) [25]. It is also known that in acidic media 1,2,4-triazin-4-oxides **7** can form adducts with arenes bearing strongly electron-donating groups ($\text{R} = \text{OR}$) (route D, Scheme 2) [26, 27]. The third possible substrates for the synthesis of **3** are halogenated triazine derivatives **8**. Studies of mono- and diazahetarenes have demonstrated that the presence of a halogen atom in an azine molecule (pyridine [28], phthalazine [29], quinazoline [30], quinolines [30]) allows to employ *ipso*-substitution reactions with arenes bearing various electron-donating groups in the presence of AlCl_3 (route E, Scheme 2), or to react the arenes with the corresponding Grignard reagents (route F, Scheme 2) [31]. Cross-coupling reactions allow to introduce a wide range of aryl substituents into halogenated azines (route G, Scheme 2) [32, 33]. However, successful cross-coupling arylation (Suzuki reaction) has been reported only for 6-bromo derivatives ($\text{R} = \text{Cl}$, CH_3 , OH), at C(6) [1]. Another noteworthy substrate for the target compounds **3** are 1,2,4-triazines **9** bearing a CCl_3 group at C(3), that undergo *tele*-



Scheme 1. Two pathways to the substituted 1,2,4-triazines.



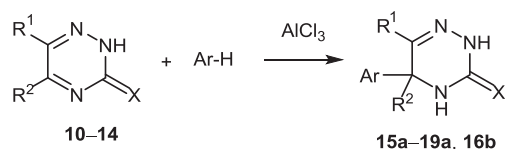
Scheme 2 (color online). The routes for the introduction of aryl substituents into azaarenes.

substitution with OH-substituted arenes, leading to the formation of triazines **3** (route H, Scheme 2) [34].

Among the described triazine precursors to aryl-triazines **3**, compounds **6** attract the highest interest due to the easier availability of most unsubstituted triazines. Recently, the arylation of 1,3,5-triazin-2,4(1*H*,2*H*)-dione, which is highly reactive towards nucleophiles, has been reported. It was demonstrated that this compound can add benzene and its derivatives with various electron-donating groups ($\text{R} = \text{CH}_3$, Cl , Br , NMe_2) in the presence of AlCl_3 [35].

Results and Discussion

In the current study, AlCl_3 -mediated reactions of arenes with a wide range of 1,2,4-triazines not bearing any additional good leaving groups were investigated. Most valuable are triazines bearing arene moieties with substituents that allow further modification. Thus, the possibility of introducing bromobenzene and toluene fragments into 1,2,4-triazines was studied. Reactions of arenes with 1,2,4-triazin-3(2*H*)-ones **10–13** and 5,6-diphenyl-1,2,4-triazin-3(2*H*)-thione (**14**) proceed with



Scheme 3.

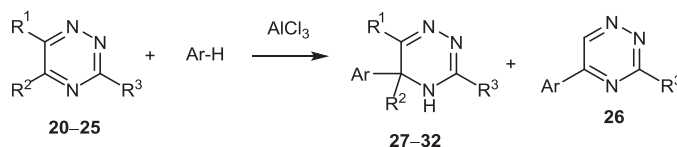
the formation of arene adducts at C(5) position of the triazine ring with 23–69% yields (Scheme 3, Table 1). Reactions with bromobenzene are too slow at room temperature, and that is why the temperature of boiling bromobenzene was used. In most cases the reaction conditions lead to the partial destruction of the triazines under formation of complex mixtures of products.

Studies of the reactions of triazines without C=O or C=S groups with arenes have shown that this reaction similarly leads generally to the formation of adducts at C(5). The only difference was observed for the reaction of 5,6-unsubstituted triazine **20** with toluene at room temperature. An oxidized product **26** was obtained, presumably due to the low stability of the formed adduct to atmospheric oxygen. The triazine **20** is very susceptible to nucleophiles, and after 18 hours of reaction it was usually not possible to obtain products of a nucleophilic addition because of decomposition reactions (Scheme 4, Table 2). Compounds **22**, **23** and **24** do not react with bromobenzene neither at 25 °C nor at 156 °C.

1,2,4-Triazines bearing an oxo group at position C(5), such as 3-Ph-1,2,4-triazin-5(4*H*)-one,

Table 1. Synthesis of 5-aryl derivatives from 1,2,4-triazin-3(2*H*)-ones and 1,2,4-triazin-3(2*H*)-thiones.

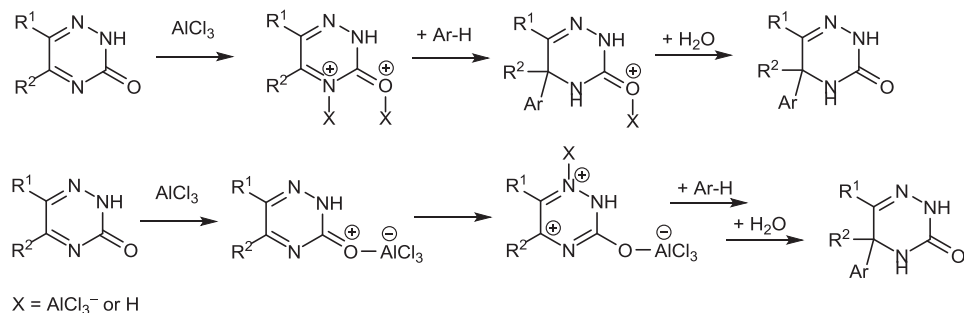
Triazine	R ¹	R ²	X	Ar	T (°C)	Time (h)	Product	Yield (%)
10	Ph	H	O	<i>p</i> -CH ₃ Ph	25	18	15a	57
				<i>p</i> -BrPh	156	1	–	mixture of products
11	<i>p</i> -CH ₃ Ph	H	O	<i>p</i> -CH ₃ Ph	25	18	16a	66
				<i>p</i> -BrPh	156	1	16b	44
12	<i>p</i> -BrPh	H	O	<i>p</i> -CH ₃ Ph	25	18	17a	63
				<i>p</i> -BrPh	156	1	–	mixture of products
13	Ph	Ph	O	<i>p</i> -CH ₃ Ph	25	18	18a	69
				<i>p</i> -BrPh	156	1	–	no reaction
14	Ph	Ph	S	<i>p</i> -CH ₃ Ph	25	18	19a	23
				<i>p</i> -BrPh	156	1	–	decomposition



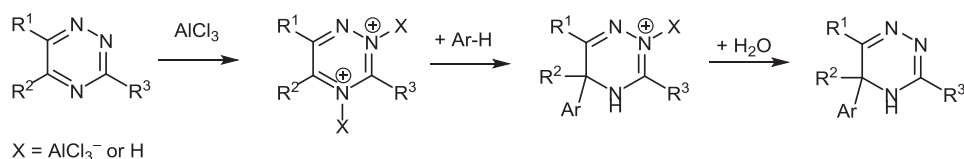
Scheme 4.

Table 2. Synthesis of 5-aryl derivatives of 1,2,4-triazines.

Triazine	R ¹	R ²	R ³	Ar	T (°C)	Time (h)	Product	Yield (%)
20	H	H	SMe	<i>p</i> -CH ₃ Ph	25	1	26	23
				<i>p</i> -BrPh	25	18	27	40
21	H	H	Ph	<i>p</i> -CH ₃ Ph	25	18	mixture	
				<i>p</i> -BrPh	25	18	28	47
22	H	Ph	CH ₃	<i>p</i> -CH ₃ Ph	25	18	29	38
23	Ph	Ph	Ph	<i>p</i> -CH ₃ Ph	25	18	30	51
24	Ph	Ph	CH ₃	<i>p</i> -CH ₃ Ph	25	18	31	61
25	<i>p</i> -CH ₃ Ph	H	Ph	<i>p</i> -CH ₃ Ph	25	18	32	73



Scheme 5. The proposed mechanism for the arylation of 1,2,4-triazin-3(2H)-ones.



Scheme 6. The proposed mechanism for the arylation of 1,2,4-triazines.

6-Ph-1,2,4-triazin-5(4H)-one or 6-Ph-1,2,4-triazin-3,5(2H,4H)-dione appeared not to be susceptible to activation with aluminum chloride at ambient temperature and at reflux in the corresponding arene. Deaza analogs of 6-Ph-1,2,4-triazin-3(2H)-one, 5-Ph-pyrimidin-2(1H)-one and 1-Me-5-Ph-pyrimidin-2(1H)-one, were also inert under the described conditions.

In the presence of strong acids, the studied triazines usually form triazinium cations, which can add strong nucleophiles, such as indoles, anilines and phenols [14, 19, 20]. It was demonstrated that activation with CF_3COOH is not sufficient to perform reactions with toluene and bromobenzene. The suggestion is that aluminum chloride in the studied process acts as a superacid [36] which leads to the conversion of 1,2,4-triazine to a dication [37–41] which is capable of reacting with arenes with the formation of dihydro-products (Schemes 5, 6).

Conclusion

In the current study a convenient method for the activation of triazines with aluminum chloride is presented, which can afford 1,2,4-triazines with different substituents at C(5) and C(6). This method is a viable alternative to the existing ones, and a number of novel

1,2,4-triazines were obtained as a result of its application.

Experimental Section

6-Ar-1,2,4-triazin-3(2H)-ones (**10–12**) [42], 5,6-diphenyl-1,2,4-triazin-3(2H)-one (**13**) [43], 5,6-diphenyl-1,2,4-triazine-3(2H)-thione (**14**) [44], 3-(methylthio)-1,2,4-triazine (**20**) [45], 3-phenyl-1,2,4-triazine (**21**) [45], 3-methyl-5-phenyl-1,2,4-triazine (**22**) [17], 3,5,6-triphenyl-1,2,4-triazine (**23**) [46], 3-methyl-5,6-diphenyl-1,2,4-triazine (**24**) [46] and 3-phenyl-6-*p*-tolyl-1,2,4-triazine (**25**) [47] were synthesized by known methods, other starting materials were commercially available. Column chromatography was performed on Merck silica gel 60. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer; tetramethylsilane (TMS) was used as an internal standard. Mass spectra were recorded on a Bruker Daltonics MicroTOF-Q II mass spectrometer with electrospray ionization.

General procedure for the synthesis of compounds **15–19a**, **16b** and **26–32**

Method A. A mixture of 300 mg of triazine (1 eqv.), anhydrous aluminum chloride (4 eqv.) and 3 mL of the corresponding arene was stirred vigorously at room temperature for 18 h. Then the reaction mixture was treated with 10 mL of cooled water, and the water layer was decanted. The organic layer was evaporated, and the resulting

residue was crystallized or chromatographed (see below for details).

Method B. A mixture of 300 mg of triazine and anhydrous aluminum chloride (4 eqv.) was refluxed in 3 mL of the corresponding arene for 1 h. For further work-up see method A.

6-Ph-5-(*p*-Tolyl)-4,5-dihydro-1,2,4-triazin-3(2H)-one (15a)

The substance was crystallized from an EtOAc-EtOH mixture. M.p. 270–272 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.23 (s, 3 H, CH₃), 5.66 (d, 1 H, *J* = 3.15 Hz, C(5)H), 7.13 (d, 2 H, *J* = 8.1 Hz, *p*-Tol), 7.19 (d, 2 H, *J* = 8.1 Hz, *p*-Tol), 7.30–7.37 (m, 3 H, Ph), 7.69–7.71 (m, 2 H, Ph), 7.98 (s, 1 H, NH), 10.23 ppm (d, 1 H, *J* = 1.9 Hz, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 21.1, 53.6, 126.1, 127.4, 129.0, 129.5, 129.9, 134.5, 137.8, 138.1, 143.8, 151.9 ppm. – HRMS ((+)-ESI): *m/z* = 266.1282 (calcd. 266.1288 for C₁₆H₁₆N₃O, [M+H]⁺).

5,6-Di-(*p*-tolyl)-4,5-dihydro-1,2,4-triazin-3(2H)-one (16a)

The substance was crystallized from an EtOAc-EtOH mixture. M.p. 260–261 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.28 (s, 3 H, CH₃), 2.30 (s, 3 H, CH₃), 5.50 (d, 1 H, *J* = 3.1 Hz, C(5)H), 7.08–7.10 (m, 4 H), 7.17 (d, 2 H, *J* = 8.0 Hz), 7.54 (d, 2 H, *J* = 8.1 Hz), 7.80 (s, 1 H, NH), 9.95 ppm (d, 1 H, *J* = 1.6 Hz, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 21.1, 21.2, 53.6, 126.1, 127.3, 129.6, 129.9, 131.8, 137.8, 138.2, 139.2, 143.8, 152.0 ppm. – HRMS ((+)-ESI): *m/z* = 280.1449 (calcd. 280.1444 for C₁₇H₁₈N₃O, [M+H]⁺).

5-(4-Bromophenyl)-6-(*p*-tolyl)-4,5-dihydro-1,2,4-triazin-3(2H)-one (16b)

The substance was crystallized from an EtOAc-EtOH mixture. M.p. 240–241 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.28 (s, 3 H, CH₃), 5.68 (d, 1 H, *J* = 3.0 Hz, C(5)H), 7.16 (d, 2 H, *J* = 8.0 Hz), 7.22–7.42 (m, 4 H), 7.61 (d, 2 H, *J* = 8.1 Hz), 7.95 (s, 1 H, NH), 10.14 ppm (s, 1 H, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 21.1, 54.3, 126.1, 127.4, 128.4, 129.3, 129.5, 132.0, 139.2, 141.1, 144.0, 151.9 ppm. – HRMS ((+)-ESI): *m/z* = 344.0389 (calcd. 344.0393 for C₁₆H₁₅BrN₃O, [M+H]⁺).

6-(4-Bromophenyl)-5-(*p*-tolyl)-4,5-dihydro-1,2,4-triazin-3(2H)-one (17a)

The substance was crystallized from an EtOAc-EtOH mixture. M.p. 261–262 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.28 (s, 3 H, CH₃), 5.54 (d, 1 H, *J* = 2.9 Hz, C(5)H), 7.09 (d, 2 H, *J* = 7.8 Hz), 7.17 (d, 2 H, *J* = 7.9 Hz), 7.43 (d, 2 H, *J* = 8.5 Hz), 7.59 (d, 2 H, *J* =

8.5 Hz), 7.95 (s, 1 H, NH), 10.14 ppm (s, 1 H, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 21.1, 53.5, 122.9, 127.3, 128.1, 130.0, 132.0, 133.7, 137.9, 138.0, 142.8, 151.6 ppm. – HRMS ((+)-ESI): *m/z* = 344.0399 (calcd. 344.0393 for C₁₆H₁₅BrN₃O, [M+H]⁺).

5-(*p*-Tolyl)-5,6-diphenyl-4,5-dihydro-1,2,4-triazin-3(2H)-one (18a)

The substance was crystallized from an EtOAc-EtOH mixture. M.p. 261–262 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.33 (s, 3 H, CH₃), 7.01–7.21 (m, 9 H), 7.21–7.34 (m, 5 H), 8.31 (s, 1 H, NH), 10.21 ppm (s, 1 H, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 19.6, 66.1, 127.1, 127.8, 127.9, 128.2, 128.4, 128.5, 128.5, 128.6, 135.6, 137.9, 138.3, 141.5, 149.1, 154.1 ppm. – HRMS ((+)-ESI): *m/z* = 342.1606 (calcd. 342.1601 for C₂₂H₂₀N₃O, [M+H]⁺).

5-(*p*-Tolyl)-5,6-diphenyl-4,5-dihydro-1,2,4-triazine-3(2H)-thione (19a)

The substance was crystallized from EtOH. M.p. 239–240 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.33 (s, 3 H), 7.03–7.24 (m, 9 H), 7.24–7.35 (m, 5 H), 9.94 (d, 1 H, *J* = 1.4 Hz, NH), 11.54 ppm (d, 1 H, *J* = 1.5 Hz, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 21.1, 64.6, 128.1, 128.5, 128.6, 129.0, 129.1, 129.2, 129.3, 135.5, 137.9, 138.3, 141.5, 148.5, 172.4 ppm. – HRMS ((+)-ESI): *m/z* = 358.1370 (calcd. 358.1372 for C₂₂H₂₀N₃S, [M+H]⁺).

3-(Methylthio)-5-*p*-tolyl-1,2,4-triazine (26)

The substance was chromatographed with EtOAc-DCM (1 : 1) as eluent. M.p. 146–148 °C. – *R*_f = 0.6. – ¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3 H, CH₃), 2.72 (s, 3 H, SCH₃), 7.34 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 8.05 (d, 2 H, *J* = 8.2 Hz, *p*-Tol), 9.33 ppm (s, 1 H, NH). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 13.9, 21.7, 127.6, 130.1, 130.3, 141.8, 143.6, 154.5, 173.6 ppm. – HRMS ((+)-ESI): *m/z* = 218.0758 (calcd. 218.0746 for C₁₁H₁₂N₃S, [M+H]⁺).

5-(4-Bromophenyl)-3-(methylthio)-4,5-dihydro-1,2,4-triazine (27)

The substance was crystallized from a CH₃CN-(CH₃)₂CHOH mixture. M.p. 185–186 °C. – ¹H NMR (400 MHz, [D₆]DMSO): δ = 2.76 (s, 3 H, SCH₃), 5.43 (d, 1 H, *J* = 2.4 Hz, C(5)H), 7.36 (d, 2 H, *J* = 8.0 Hz), 7.56 (d, 1 H, *J* = 2.4 Hz), 7.68 (d, 2 H, *J* = 8.0 Hz), 12.94 ppm (br.s, 1H). – ¹³C NMR (100 MHz, [D₆]DMSO): δ = 13.7, 50.9, 122.2, 129.1, 132.0, 136.3, 144.4, 160.4 ppm. – HRMS ((+)-ESI): *m/z* = 283.9846 (calcd. 283.9852 for C₁₀H₁₁BrN₃S, [M+H]⁺).

5-(4-Bromophenyl)-3-Ph-4,5-dihydro-1,2,4-triazine (28)

The substance was crystallized from CH_3CN . M. p. 185–186 °C. – ^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$): δ = 5.63 (d, 1 H, J = 3.0 Hz, C(5)H), 7.47 (m, 2 H), 7.65–7.73 (m, 4 H), 7.79–7.83 (m, 1 H), 7.95–7.99 (m, 2 H), 12.16 (br.s, 1 H), 13.54 ppm (br.s, 1 H). – ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 50.3, 123.1, 125.0, 129.5, 129.6, 130.1, 132.7, 135.2, 137.3, 145.9, 154.6 ppm. – HRMS ((+)-ESI): m/z = 314.0293 (calcd. 314.0287 for $\text{C}_{15}\text{H}_{13}\text{BrN}_3$, $[\text{M}+\text{H}]^+$).

3-Me-5-Ph-5-(p-tolyl)-4,5-dihydro-1,2,4-triazine (29)

The substance was chromatographed with EtOAc-DCM (1 : 1) as eluent. M. p. 130–131 °C. – R_f = 0.5. – ^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$): δ = 2.32 (s, 3 H, CH_3), 2.44 (s, 3 H, CH_3), 7.09–7.14 (m, 5 H), 7.23–7.27 ppm (m, 5 H). – ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 16.3, 21.1, 60.3, 127.3 (2C), 128.8, 129.0, 129.8, 137.7, 138.9, 140.7, 145.2, 154.8 ppm. – HRMS ((+)-ESI): m/z = 264.1495 (calcd. 264.1495 for $\text{C}_{17}\text{H}_{18}\text{N}_3$, $[\text{M}+\text{H}]^+$).

3,5,6-Triphenyl-5-(p-tolyl)-4,5-dihydro-1,2,4-triazine (30)

The substance was crystallized from EtOH. M. p. 185–186 °C. – ^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$): δ = 2.35 (s, 3 H, CH_3), 7.18–7.23 (m, 4 H), 7.28–7.42 (m, 9 H), 7.59–7.63 (m, 2 H), 7.74–7.78 (m, 1 H), 8.02–8.04 (m, 2 H), 12.23 (s, 1 H), 14.50 ppm (br.s, 1 H). – ^{13}C NMR

(100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 21.1, 64.0, 128.5, 129.1, 129.4, 129.5, 129.8, 129.9, 130.5, 130.8, 133.8, 135.2, 135.3, 139.0, 153.3 ppm. – HRMS ((+)-ESI): m/z = 402.1956 (calcd. 402.1965 for $\text{C}_{28}\text{H}_{24}\text{N}_3$, $[\text{M}+\text{H}]^+$).

3-Methyl-5,6-diphenyl-5-(p-tolyl)-4,5-dihydro-1,2,4-triazine (31)

The substance was crystallized from an EtOH-EtOAc mixture. M. p. 236 °C. – ^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$): δ = 2.35 (s, 3 H), 2.44 (s, 3 H), 7.14–7.21 (m, 4 H), 7.25–7.29 (m, 5 H), 7.35–7.40 (m, 5 H), 12.42 ppm (s, 1 H). – ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 16.1, 21.0, 63.5, 128.4, 129.0, 129.1, 129.2, 129.3, 129.7, 130.5, 134.1, 137.1, 138.9, 140.2, 150.6, 155.3 ppm. – HRMS ((+)-ESI): m/z = 340.1795 (calcd. 340.1808 for $\text{C}_{23}\text{H}_{22}\text{N}_3$, $[\text{M}+\text{H}]^+$).

3-Phenyl-5,6-di(p-tolyl)-4,5-dihydro-1,2,4-triazine (32)

The substance was crystallized from a large amount of acetone. M. p. 239 °C. – ^1H NMR (400 MHz, $[\text{D}_6]\text{DMSO}$): δ = 2.31 (s, 3 H), 2.38 (s, 3 H), 6.19 (s, 1 H, C(5)H), 7.20 (d, 2 H, J = 7.8 Hz), 7.25 (d, 2 H, J = 8.0 Hz), 7.38 (d, 2 H, J = 7.8 Hz), 7.60–7.64 (m, 2 H), 7.74–7.78 (m, 1 H), 7.81 (d, 2 H, J = 8.0 Hz), 8.02 (d, 2 H, J = 7.8 Hz), 12.87 (br.s, 1 H, NH), 13.80 (br.s, 1 H, NH). – ^{13}C NMR (100 MHz, $[\text{D}_6]\text{DMSO}$): δ = 20.6, 20.9, 49.4, 124.2, 127.0, 127.3, 128.8, 129.0, 129.2, 129.5, 129.9, 134.6, 134.6, 138.9, 141.9, 150.0, 152.4. – HRMS ((+)-ESI): m/z = 340.1811 (calcd. 340.1808 for $\text{C}_{23}\text{H}_{22}\text{N}_3$, $[\text{M}+\text{H}]^+$).

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